Risk factors for physical disability in patients with leprosy: a systematic review and meta-analysis

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Word count (manuscript): 2,120

Date of the revision: April 18, 2019

Abstract

Importance: The World Health Organization (WHO) 2016–2020 Global Leprosy Strategy aims to reinvigorate efforts to control leprosy and avert leprosy disability to less than one per million population.

Objective: This study aimed to identify systematically clinical factors associated with physical disability in patients with leprosy.

Data source: Searches were performed in Scopus, PubMed and Web of Science databases to identify studies published up to May 2018, using the keywords *leprosy* and *physical disability* and related terms.

Study selection: We included studies that evaluated patients using the WHO leprosy disability grading and reported the number of patients with and without disability by clinical characteristics.

Data Extraction and Synthesis: The study was conducted following the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) statement. We used the odds ratio (OR) as a measure of association between the clinical features and physical disability. Summary estimates were calculated using random-effects models.

Main Outcome(s) and Measure(s): Our primary outcome was physical disability according the WHO disability classification. We evaluated the association between clinical features and physical disability.

Results: Thirty-two studies were included in the systematic review. Males were more likely to have physical disability than females (pooled OR: 1.66; CI95% 1.43-1.93). Multibacillary (MB) leprosy were 4-fold more likely to have physical disability than paucibacillary (PB) leprosy

patients (pooled OR 4.32; CI95% 3.37-5.53). Patients having leprosy reactions were more likely to have disability (pooled OR 2.43, CI95% 1.35-4.36). Patients with lepromatous leprosy experienced 5- to 12-fold higher odds of disability.

Conclusion and Relevance: This systematic review and meta-analysis confirms the strong association between the presence of physical disabilities and male gender, MB leprosy, leprosy reactions and lepromatous presentation. These findings can guide the development of targeted interventions to identify early individuals at greater risk of developing physical disabilities and education campaigns to promote early consultation to institute treatment for leprosy reactions and to prevent physical disability.

Key-words: Leprosy, Physical disability, Risk factors, Systematic review, Meta-analysis.

Key points

Question: What are the risk factors for physical disability in patients with leprosy?

Findings: This systematic review and meta-analysis found a strong association between the presence of physical disabilities and male gender, MB leprosy, leprosy reactions and lepromatous presentation.

Meaning: Our findings can guide the early identification of individuals at higher risk of developing physical disabilities and the development of targeted preventive interventions.

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that affects the skin and peripheral nerves leading to progressive physical disability and deformities if not diagnosed and treated early.[1–3] Despite a significant reduction in its global prevalence since the World Health Organization (WHO) implemented the free multidrug therapy program in 1995, leprosy remains a major cause of morbidity due to its associated long term disabilities and sequelae[4] affecting an estimated two million people worldwide.[5,6]

The WHO target is to reduce leprosy disabilities to less than one per million population through the strengthening of strategies for the prevention and reduction of deformities.[7] These strategies include the early recognition and prioritization of individuals with characteristics associated with physical disability and the main focus of control programs and rehabilitation centers is to prevent and manage physical impairment to improve quality of life.[8,9] Although clinical features such as multibacillary (MB) leprosy and leprosy reactions are considered to predispose to physical disability and deformity,[2,5,10–13] there are no systematic analyses assessing the strength of this evidence. We report here a systematic review and meta-analysis to assess the clinical factors associated with physical disability in leprosy.

Methods

This study was conducted following the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) statement.[14] Institutional review board approval and informed consent were not required as all data were obtained from secondary data sources without identifiers. The study protocol was designed a priori and registered in the PROSPERO database (registration number CRD 42019118122).

Search strategy and selection criteria

We systematically searched the PubMed, Scopus and Web of Science databases to identify studies published up to May 2018, using the keywords *leprosy* and *physical disability* and related terms, as described in eTable 1 of the supplement. Two independent reviewers (HLP and CDFS) screened the search results and identified potentially relevant studies based on their title and abstract. The studies were then read in full for consideration for inclusion in the analysis. Disagreements between the two reviewers were resolved by discussion. Studies were included if a) patients had been assessed for physical disability using the WHO leprosy disability grading[1]; b) the study evaluated the association between the clinical presentation and physical disability; and c) the clinical factors (exposure) were described according to the presence or absence of physical disability. We excluded publications without original data such as reviews and opinions, those with overlapping data or when data extraction was not possible. The authors of the latter studies were asked to provide access to the original databases, but none of them responded.

We considered age, sex, clinical presentation categories, the presence of leprosy reactions and the WHO leprosy classification stage as exposure factors. The WHO classification includes paucibacillary (PB, ≤5 skin lesions and/or only one affected nerve trunk) and multibacillary (MB, >5 skin lesions and/or more than one affected nerve trunk) leprosy or based on smear microscopy findings into PB leprosy, if smear negative, or MB leprosy, if smear positive.[15] Clinical forms include tuberculoid, borderline or lepromatous and indeterminate presentations.[16] Leprosy reactions include episodes characterized by the acute inflammation of

skin lesions or nerves (type 1) and/or the appearance of inflamed cutaneous nodules with or without neuritis (type 2).[17]

Our primary outcome was physical disability according to the WHO disability classification.[1] In this classification, grade 0 indicates no sensory impairment or disability/damage of the eyes, hands or feet; grade 1 indicates the presence of eye (vision >6/60) or sensory impairment in the hands or feet, without visible deformities or damages; grade 2 indicates severe visual impairment (vision <6/60 or inability to count fingers at six meters) or the presence of visible deformity in the eyes (lagophthalmos, iridocyclitis and corneal opacities) or visible deformity or damage on hands or feet (ulcerations, traumatic injuries, resorption, claw, fallen hand, foot drop, ankle contracture). We combined physical disability grades 1 and 2 and considered them jointly for statistical purposes.

Data extraction and bias assessment

Data were extracted using standardized tables, including author, country, study design, participants characteristics, clinical setting (specialized health center, general hospital, primary health care or data obtained from a health information system) and physical disability (presence or absence). We extracted the number of cases with and without physical disability at the time of diagnosis and stratified for each exposure variable. Not all studies reported all variables and we used percentages to obtain the absolute number of patients by stratum.

The Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies of the USA National Institutes of Health (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools) was used to grade the quality of each study. Disagreements were resolved by discussion.

Statistical analysis

We calculated the pooled odds ratio (OR) for the primary outcome and forest plots to present results with 95% confidence intervals (95% CI). Not all studies reported data on all exposure variables and the pooled OR was estimated from the data available for each variable. Pooled estimates were calculated using a random-effects model (DerSimonian and Laird method). Two-tailed p-values <0.05 were used to determine statistical significance. Statistical heterogeneity was assessed using the Cochran's Q test[18] and quantified by the I^2 index.[19]

Subgroup analysis were performed according to the study design, population characteristics (adults, adults/children and children) and study setting. Publication bias was assessed by visually inspecting whether larger and smaller studies were asymmetrically distributed in the funnel plot.[20] Leave-one-out sensitivity analysis was conducted to examine the influence of each study on the pooled effect size.[21] Analyses were performed using STATA 14.0 (STATA Corp., College Station, TX, USA) and Review Manager 5.3 (Cochrane IMS, Copenhagen, Denmark).

Results

The search strategy identified 2,447 reports. After screening titles and abstracts, 177 full-text articles were assessed for eligibility and 32 were included in the analysis (Figure 1). Table 1 describes the characteristics of the studies included. Most studies were cross-sectional (27, 84.4%), four (12.5%) were from surveillance systems (continuous and routine reporting of cases for monitoring purposes) and only one (3.1%) was a cohort. Nine (28.1%) studies included adults, three (9.4%) included children and 20 (62.5%) enrolled both adults and children and reported them combined. Eleven (34.4%) studies were based in general hospitals, nine (28.1%)

in primary health care settings and eight (25.0%) in specialized health care centers, while four (12.5%) were data extracted from health information systems and the origin of the patients was not reported.

The risk of bias of the studies is showed in eTable 2 in the supplement. All studies had clear objectives and eligibility criteria, recruited subjects from the same population and described the definitions of exposure factors and outcomes. However, most studies did not report the number of eligible participants recruited into the study. Since most studies were cross-sectional, the exposure and outcome status (physical disability) of the participants were collected at the same time, which are potential sources of bias.

Twenty-four studies had sex information (39,571 patients), of which 24,218 (61.2%) were male and 15,353 (38.8%) female.[2,5,10–13, 22–38] Males were more likely to have physical disability than females (pooled OR: 1.66; 95% CI: 1.43-1.93; I^2: 81.3%, P: <0.001) and the odds of physical disability did not depend on the study location (Figure 2).

WHO leprosy classification data were obtained from 28 studies including 39,192 patients.[2,5,10,11,13,22,23,25–29,31–35,37–47] PB leprosy was more frequent than MB leprosy [25,954 (66.2%) and 13,238 (33.8%), respectively], but patients with MB leprosy were 4-fold more likely to have physical disabilities (pooled OR: 4.32; 95% CI: 3.37-5.53; I^2: 88.9%, P: <0.001) independently of the study location (Figure 3).

Six studies reported leprosy reactions and disability,[2,11,37,38,42,43] including 9,691 patients, of whom 1,694 (17.5%) had leprosy reactions and 7,997 (82.5%) no reactions, resulting a pooled OR of 2.43 (95% CI: 1.35-4.36; I^2: 92.1%, P: <0.001) (Figure 4). The clinical presentation was reported in seven studies. Patients with lepromatous forms were more likely to have disability

than patients with borderline (pooled OR: 2.94, 95% CI: 1.72-5.02; I^2: 92.2%, P: <0.001), tuberculoid (pooled OR: 5.85, 95% CI: 3.56-9.61; I^2: 90.8%, P: <0.001) or indeterminate leprosy (pooled OR: 12.53, 95% CI: 6.34-24.76; I^2: 86.4%, P: <0.001) and these pooled ORs were not dependent on the study location (Figure 5).

Sensitivity analysis suggested the pooled ORs were stable and not obviously changed by a single study. No evidence of publications bias was observed (see eFigures 7-11 in the Supplement).

Discussion

Factors predisposing to the development of physical disability in leprosy have been reported extensively, providing an excellent opportunity for a comprehensive analysis. This review confirms that male patients, those with MB leprosy, leprosy reactions and lepromatous presentations are more likely to have physical disabilities.

Men were almost 2-times more likely to have physical disability than women. This gender difference has been attributed to social behaviors and reluctance and difficulties in accessing health services.[48] Men often ignore leprosy symptoms and seek health services at more advanced stages of the disease and with more severe clinical manifestations.[49–51] Health professionals should be aware of their increased risk during active case finding activities and contact tracing, to ensure male contacts and secondary cases are not missed during home visits.

Leprosy disease progression is determined by the cellular immune responses to *M. leprae*, which are expressed through different pathophysiological mechanisms. The absence of cellular and enhanced humoral immune responses of patients with MB leprosy are associated with high bacilli loads and result in neuritis and peripheral nerve damage.[26,52] Patients with MB

leprosy in this review were more likely to have physical disabilities, highlighting the importance of good clinical classification and the smear microscopy detection of bacilli.[16]

Although tuberculoid and indeterminate leprosy are the most frequent clinical presentations, our meta-analysis demonstrates that patients with lepromatous leprosy have 5- to 12-fold higher odds of disability. Lepromatous leprosy is characterized by T helper cell 2 immune responses with increased production of IL-4 and IL-10 and activation of regulatory T cells, a robust, but ineffective, production of antibodies with formation of immune complexes, and a failure to restrict *M. leprae* growth, especially into the Schwann cells.[53] The immunological events triggered against infected Schwann cells then results in nerve injuries and consequent physical disability.[54]

Individuals with leprosy reactions are more prone to peripheral nerve injuries and sequelae. Type 1 reactions are a reversal or upgrade of the cell-mediated immunity to *M. leprae* antibodies, while type 2 reactions are the result of immune complexes attracting granulocytes and activation of complement and cytokine responses.[53] Both reactions may damage peripheral nerves with impairment of function and can occur at any time in the clinical course of the disease, independently of treatment. It is thus recommended to follow leprosy cases for several years after an apparently successful treatment.[4,55,56]

This systematic review focused on the likelihood of disability among patients with leprosy reactions at the time of diagnosis. However, studies have reported a high risk of leprosy reactions after completion of MDT treatment, requiring long-term follow-up with repeated neurological examinations.[4,10,57] The early identification of reactions and their prompt

225 management with prednisone (1 to 2 mg/kg/day for ≥90 days) can prevent neuropathies and
226 disability.[17]
227 The Global Leprosy Strategy 2010-2020 aims to accelerate action towards a leprosy-free world,
228 with a focus on the early detection of cases, before disabilities occur, and the prevention and
229 early detection of disabilities among higher risk groups by conducting active cases finding
230 campaigns in highly endemic areas or communities.[7] In this sense, our findings provide
231 information to stakeholders regarding to the characterization of high risk patients that should
232 be prioritized and targeted to receive preventive interventions for the early detection and
233 reduction of grade 2 disability in endemic areas.
234 Our findings however should be interpreted with caution. All studies included were
235 observational and patients were not randomized and were often conducted with other primary
236 objectives and therefore the studies are prone to patient selection bias and the disability
237 information may not have been collected systematically. Moreover, it was not possible to
238 perform meta-analyses to explore whether age, schooling level and socioeconomic status were
239 associated with physical disability. Most studies, however, indicated the prevalence of disability
240 increases with age and that disability is inversely proportional to socioeconomic conditions and
241 educational level. Education and income are considered determining factors for disease
242 improvement and protective for the occurrence of disability.[2]
243 Despite these limitations, we demonstrate a strong association between the presence of
244 physical disabilities and gender, MB leprosy, leprosy reactions and a lepromatous presentation.
245 These findings can guide the development of targeted interventions to identify early individuals
246 at risk of physical disabilities and to inform education campaigns promoting early consultation

to institute treatment for leprosy reactions and prevention of further physical disability. Long-term follow-up is necessary to monitor factors associated with disabilities, and the provision of interventions promoting self-care, disability prevention and availability of rehabilitation services.

Acknowledgments: de Paula and Dr. Santos had full access to all the data included in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest Disclosures: None reported.

Funding/Support: No funding

Role of the Funder/Sponsor: The study did not receive financial support.

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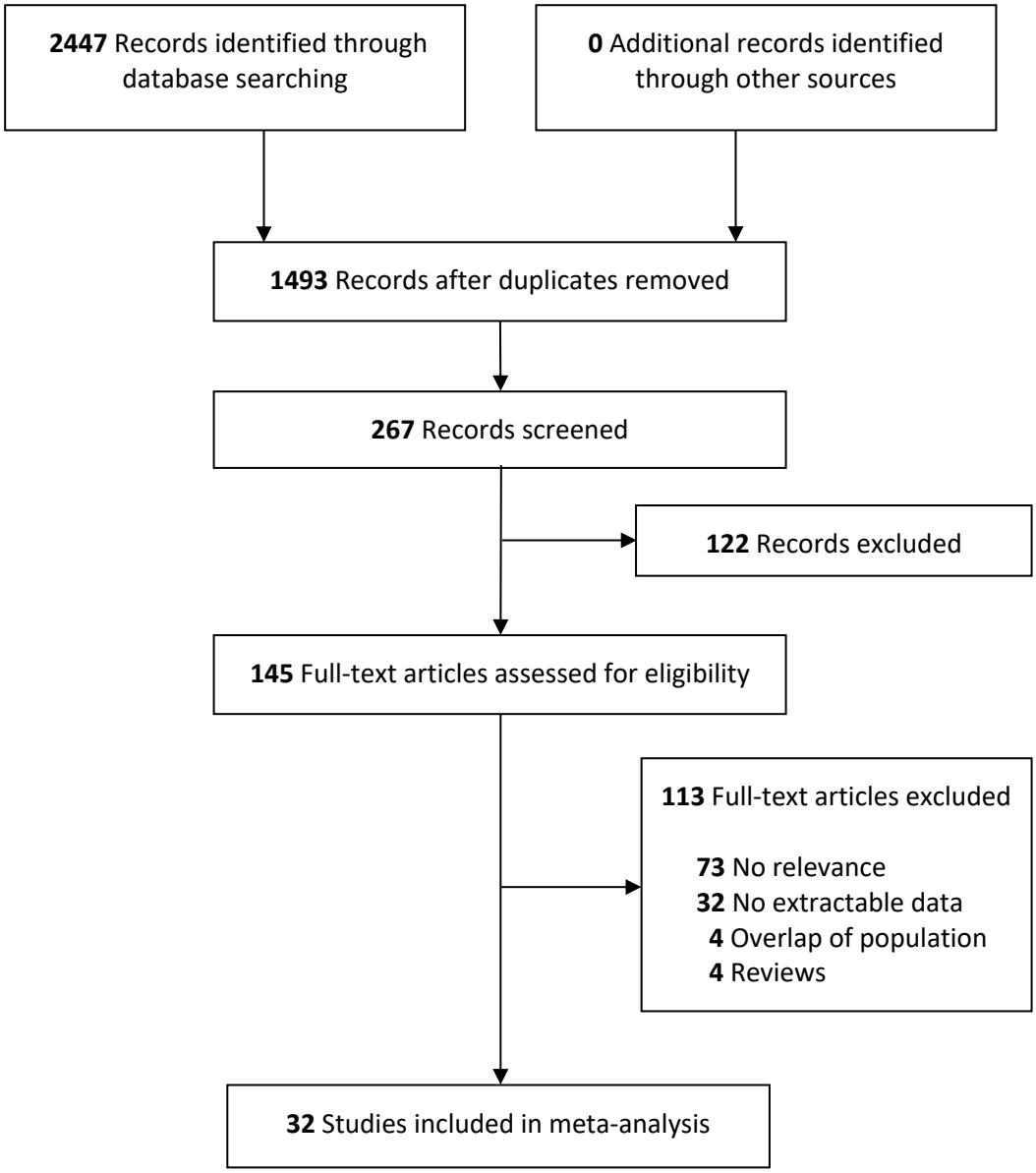
List of figures

445 **Table 1. Characteristics of the included studies.**

Study	Country	Study design	Population	Settings	Risk factors analyzed	Outcome	Sample size	Total disability
Zhang et al, 1993	China	Cross sectional	Adults/ children	Tertiary Health Centre	Sex, WHO leprosy classification and clinical forms	Combined grades 1 and 2	14257	8122
Tiendrebeogo et al, 1996	Burkina Faso	Cross sectional	Adults	Primary care	Sex and WHO leprosy classification	Combined grades 1 and 2	554	165
Çakiner et al, 1997	Turkey	Cross sectional	Adults	Hospital	Sex	Combined grades 1 and 2	711	546
Wittenhorst et al, 1998	Zimbabwe	Surveillance	Adults/ children	Information system	Sex and WHO leprosy classification	Grade 2	746	247
Croft et al, 1999	Bangladesh	Cross sectional	Adults/ children	Tertiary Health Centre	Sex and WHO leprosy classification	Combined grades 1 and 2	2664	415
Ahmad et al, 2004	Pakistan	Cross sectional	Adults	Hospital	Sex, WHO leprosy classification and clinical forms	Combined grades 1 and 2	100	41
Kar et al, 2005	India	Cross sectional	Children	Tertiary Health Centre	Sex, WHO leprosy classification and leprosy reaction	Grade 2	275	29
Rad, 2007	Iran	Cross sectional	Adults/ children	Hospital	Sex and WHO leprosy classification	Combined grades 1 and 2	180	79
Silva-Sobrinho et al, 2007	Brazil	Cross sectional	Adults/ children	Primary care	Sex	Combined grades 1 and 2	99	79
Lana et al, 2008	Brazil	Surveillance	Adults/ children	Information system	Sex and WHO leprosy classification	Combined grades 1 and 2	1461	672
Soomro et al, 2008	Pakistan	Cross sectional	Adults	Hospital	WHO leprosy classification	Separately grades 1 and 2	100	55
Ramos et al, 2010	Brazil	Cross sectional	Adults	Tertiary Health Centre	Sex and WHO leprosy classification	Separately grades 1 and 2	193	51

El-Dawela et al, 2012	Egypt	Cross sectional	Adults/ children	Hospital	WHO leprosy classification	Grade 2	587	204
Sarkar et al,2012	India	Cross sectional	Adults	Hospital	WHO leprosy classification	Separately grades 1 and 2	244	244
Kumar et al, 2012	India	Cohort	Adults/ children	Tertiary Health Centre	Sex, WHO leprosy classification and clinical forms	Grade 2	293	27
Nardi et al, 2012	Brazil	Cross sectional	Adults/ children	Primary care	Sex, WHO leprosy classification and clinical forms	Separately grades 1 and 2	335	71
van Brakel et al, 2012	Indonesia	Cross sectional	Adults	Primary care	Sex and WHO leprosy classification	Separately grades 1 and 2	1308	1003
Monteiro et al, 2013	Brazil	Cross sectional	Adults/ children	Primary care	WHO leprosy classification and leprosy reaction	Separately grades 1 and 2	282	44
Oliveira et al, 2013	Brazil	Cross sectional	Adults/ children	Tertiary Health Centre	Sex	Separately grades 1 and 2	494	142
Guerrero et al, 2013	Colombia	Cross sectional	Adults/ children	Primary care	Sex and WHO leprosy classification	Combined grades 1 and 2	333	117
de Castro et al, 2014	Brazil	Cross sectional	Adults	Primary care	Sex and WHO leprosy classification	Combined grades 1 and 2	225	137
Silva et al, 2015	Brazil	Cross sectional	Adults/ children	Primary care	Sex and WHO leprosy classification	Grade 2	1916	366
Monteiro et al, 2015	Brazil	Surveillance	Adults/ children	Information system	Sex, WHO leprosy classification, leprosy reaction and clinical forms	Grade 2	12328	664
Santos et al, 2015	Brazil	Surveillance	Adults/ children	Information system	Sex, WHO leprosy classification, leprosy reaction and clinical forms	Combined grades 1 and 2	2358	656
Sethi et al, 2015	India	Cross	Children	Hospital	WHO leprosy	Separately	94	32

		sectional			classification and clinical forms	grades 1 and 2		
Patel et al, 2016	India	Cross sectional	Adults	Tertiary Health Centre	Sex, WHO leprosy classification and leprosy reaction	Separately grades 1 and 2	239	127
Onyeonoro et al, 2016	India	Cross sectional	Adults/ children	Hospital	Sex and WHO leprosy classification	Separately grades 1 and 2	287	168
Queirós et al, 2016	Brazil	Cross sectional	Adults/ children	Hospital	WHO leprosy classification	Separately grades 1 and 2	458	63
Anjum et al, 2017	India	Cross sectional	Adults/ children	Tertiary Health Centre	WHO leprosy classification	Combined grades 1 and 2	54	48
Rodrigues et al, 2017	Brazil	Cross sectional	Adults/ children	Hospital	Sex and WHO leprosy classification	Combined grades 1 and 2	182	124
Darlong et al, 2017	India	Cross sectional	Children	Hospital	WHO leprosy classification	Grade 2	319	21
Haefner et al, 2017	Brazil	Cross sectional	Adults/ children	Primary care	Sex	Separately grades 1 and 2	910	262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113 Full-text articles excluded
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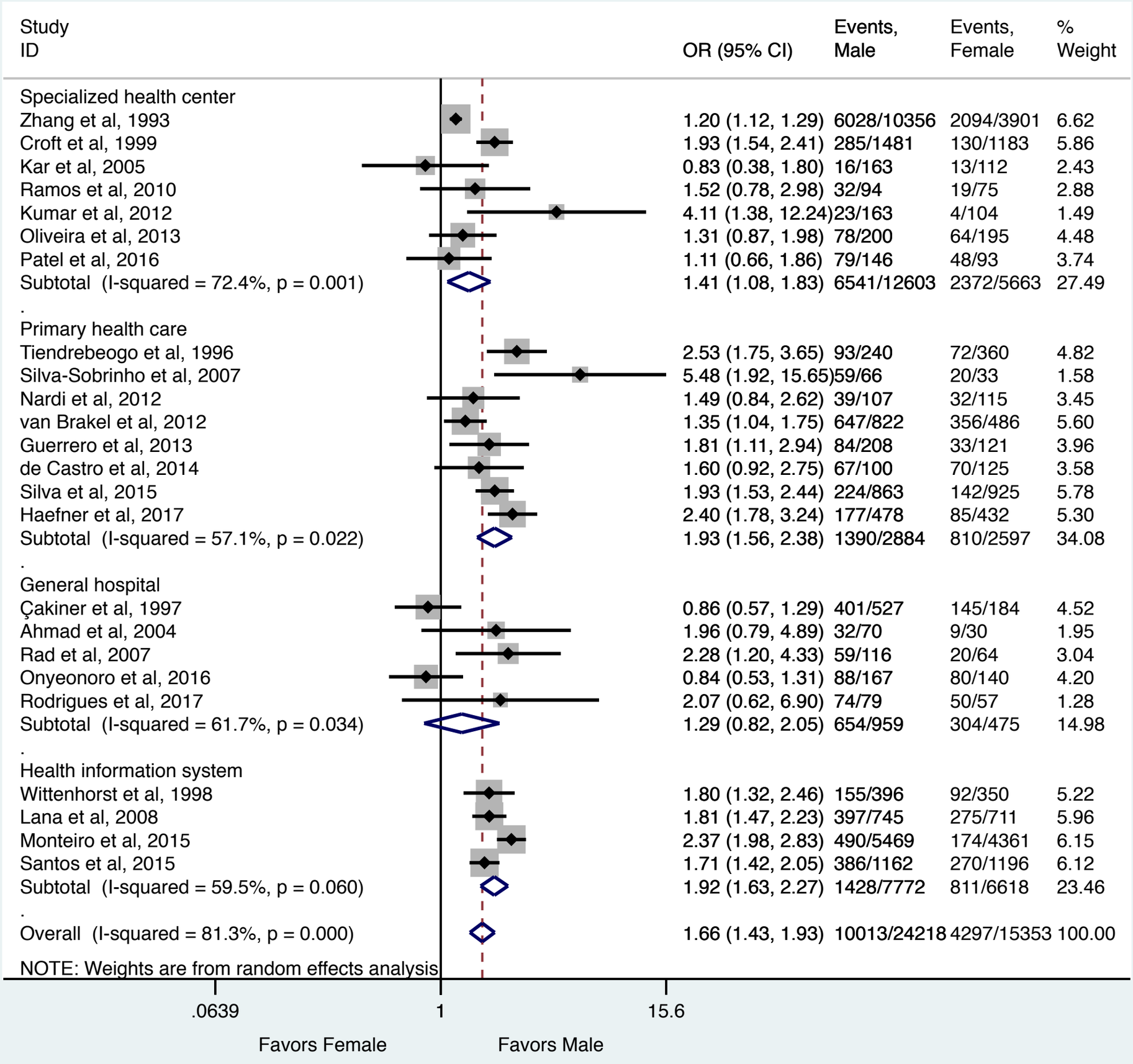
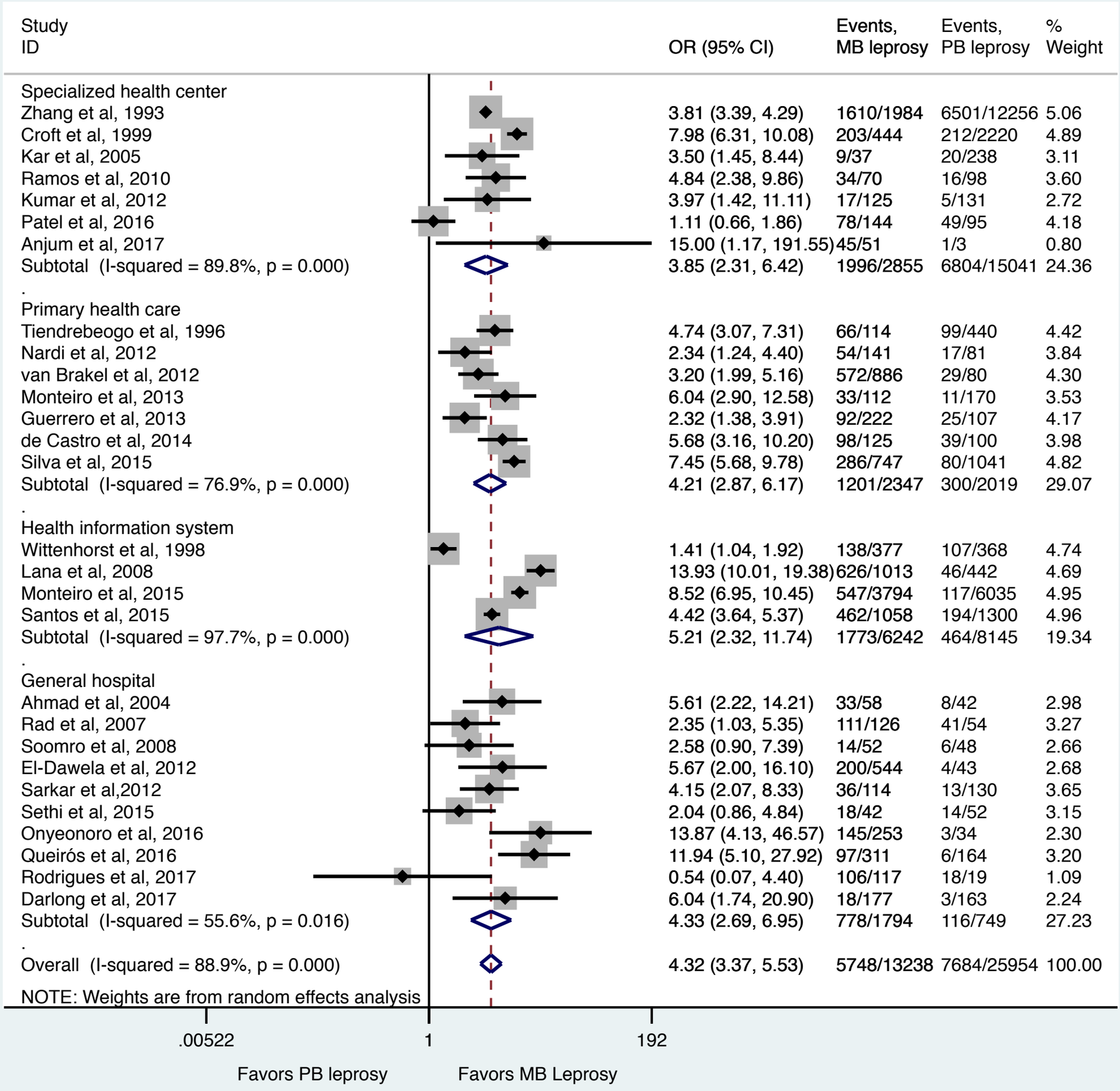
32 No extractable data
4 Overlap of population
4 Reviews
32 Studies included in meta-analysis


Study ID
OR (95% CI)
Events, Male
Events, Female
% Weight
Specialized health center
Zhang et al, 1993 1.20 (1.12, 1.29) 6028/10356 2094/3901 6.62
Croft et al, 1999 1.93 (1.54, 2.41) 285/1481 130/1183 5.86
Kar et al, 2005 0.83 (0.38, 1.80) 16/163 13/112 2.43
Ramos et al, 2010 1.52 (0.78, 2.98) 32/94 19/75 2.88
Kumar et al, 2012 4.11 (1.38, 12.24) 23/163 4/104 1.49
Oliveira et al, 2013 1.31 (0.87, 1.98) 78/200 64/195 4.48
Patel et al, 2016 1.11 (0.66, 1.86) 79/146 48/93 3.74
Subtotal (I-squared = 72.4%, p = 0.001) 1.41 (1.08, 1.83) 6541/12603 2372/5663 27.49
Primary health care
Tiendrebeogo et al, 1996 2.53 (1.75, 3.65) 93/240 72/360 4.82
Silva-Sobrinho et al, 2007 5.48 (1.92, 15.65) 59/66 20/33 1.58
Nardi et al, 2012 1.49 (0.84, 2.62) 39/107 32/115 3.45
van Brakel et al, 2012 1.35 (1.04, 1.75) 647/822 356/486 5.60
Guerrero et al, 2013 1.81 (1.11, 2.94) 84/208 33/121 3.96
de Castro et al, 2014 1.60 (0.92, 2.75) 67/100 70/125 3.58
Silva et al, 2015 1.93 (1.53, 2.44) 224/863 142/925 5.78
Haefner et al, 2017 2.40 (1.78, 3.24) 177/478 85/432 5.30
Subtotal (I-squared = 57.1%, p = 0.022) 1.93 (1.56, 2.38) 1390/2884 810/2597 34.08
General hospital
Çakiner et al, 1997 0.86 (0.57, 1.29) 401/527 145/184 4.52
Ahmad et al, 2004 1.96 (0.79, 4.89) 32/70 9/30 1.95
Rad et al, 2007 2.28 (1.20, 4.33) 59/116 20/64 3.04
Onyeonoro et al, 2016 0.84 (0.53, 1.31) 88/167 80/140 4.20
Rodrigues et al, 2017 2.07 (0.62, 6.90) 74/79 50/57 1.28
Subtotal (I-squared = 61.7%, p = 0.034) 1.29 (0.82, 2.05) 654/959 304/475 14.98
Health information system
Wittenhorst et al, 1998 1.80 (1.32, 2.46) 155/396 92/350 5.22
Lana et al, 2008 1.81 (1.47, 2.23) 397/745 275/711 5.96
Monteiro et al, 2015 2.37 (1.98, 2.83) 490/5469 174/4361 6.15
Santos et al, 2015 1.71 (1.42, 2.05) 386/1162 270/1196 6.12
Subtotal (I-squared = 59.5%, p = 0.060) 1.92 (1.63, 2.27) 1428/7772 811/6618 23.46
Overall (I-squared = 81.3%, p = 0.000) 1.66 (1.43, 1.93) 10013/24218 4297/15353 100.00
NOTE: Weights are from random effects analysis
.0639
1
15.6
Favors Female
Favors Male


Study ID
OR (95% CI)
Events, MB leprosy
Events, PB leprosy
% Weight
Specialized health center
Zhang et al, 1993 3.81 (3.39, 4.29) 1610/1984 6501/12256 5.06
Croft et al, 1999 7.98 (6.31, 10.08) 203/444 212/2220 4.89
Kar et al, 2005 3.50 (1.45, 8.44) 9/37 20/238 3.11
Ramos et al, 2010 4.84 (2.38, 9.86) 34/70 16/98 3.60
Kumar et al, 2012 3.97 (1.42, 11.11) 17/125 5/131 2.72
Patel et al, 2016 1.11 (0.66, 1.86) 78/144 49/95 4.18
Anjum et al, 2017 15.00 (1.17, 191.55) 45/51 1/3 0.80
Subtotal (I-squared = 89.8%, p = 0.000) 3.85 (2.31, 6.42) 1996/2855 6804/15041 24.36
.
Primary health care
Tiendrebeogo et al, 1996 4.74 (3.07, 7.31) 66/114 99/440 4.42
Nardi et al, 2012 2.34 (1.24, 4.40) 54/141 17/81 3.84
van Brakel et al, 2012 3.20 (1.99, 5.16) 572/886 29/80 4.30
Monteiro et al, 2013 6.04 (2.90, 12.58) 33/112 11/170 3.53
Guerrero et al, 2013 2.32 (1.38, 3.91) 92/222 25/107 4.17
de Castro et al, 2014 5.68 (3.16, 10.20) 98/125 39/100 3.98
Silva et al, 2015 7.45 (5.68, 9.78) 286/747 80/1041 4.82
Subtotal (I-squared = 76.9%, p = 0.000) 4.21 (2.87, 6.17) 1201/2347 300/2019 29.07
.
Health information system
Wittenhorst et al, 1998 1.41 (1.04, 1.92) 138/377 107/368 4.74
Lana et al, 2008 13.93 (10.01, 19.38) 626/1013 46/442 4.69
Monteiro et al, 2015 8.52 (6.95, 10.45) 547/3794 117/6035 4.95
Santos et al, 2015 4.42 (3.64, 5.37) 462/1058 194/1300 4.96
Subtotal (I-squared = 97.7%, p = 0.000) 5.21 (2.32, 11.74) 1773/6242 464/8145 19.34
.
General hospital
Ahmad et al, 2004 5.61 (2.22, 14.21) 33/58 8/42 2.98
Rad et al, 2007 2.35 (1.03, 5.35) 111/126 41/54 3.27
Soomro et al, 2008 2.58 (0.90, 7.39) 14/52 6/48 2.66
El-Dawela et al, 2012 5.67 (2.00, 16.10) 200/544 4/43 2.68
Sarkar et al,2012 4.15 (2.07, 8.33) 36/114 13/130 3.65
Sethi et al, 2015 2.04 (0.86, 4.84) 18/42 14/52 3.15
Onyeonoro et al, 2016 13.87 (4.13, 46.57) 145/253 3/34 2.30
Queirós et al, 2016 11.94 (5.10, 27.92) 97/311 6/164 3.20
Rodrigues et al, 2017 0.54 (0.07, 4.40) 106/117 18/19 1.09
Darlong et al, 2017 6.04 (1.74, 20.90) 18/177 3/163 2.24
Subtotal (I-squared = 55.6%, p = 0.016) 4.33 (2.69, 6.95) 778/1794 116/749 27.23
.
Overall (I-squared = 88.9%, p = 0.000) 4.32 (3.37, 5.53) 5748/13238 7684/25954 100.00
NOTE: Weights are from random effects analysis
.00522
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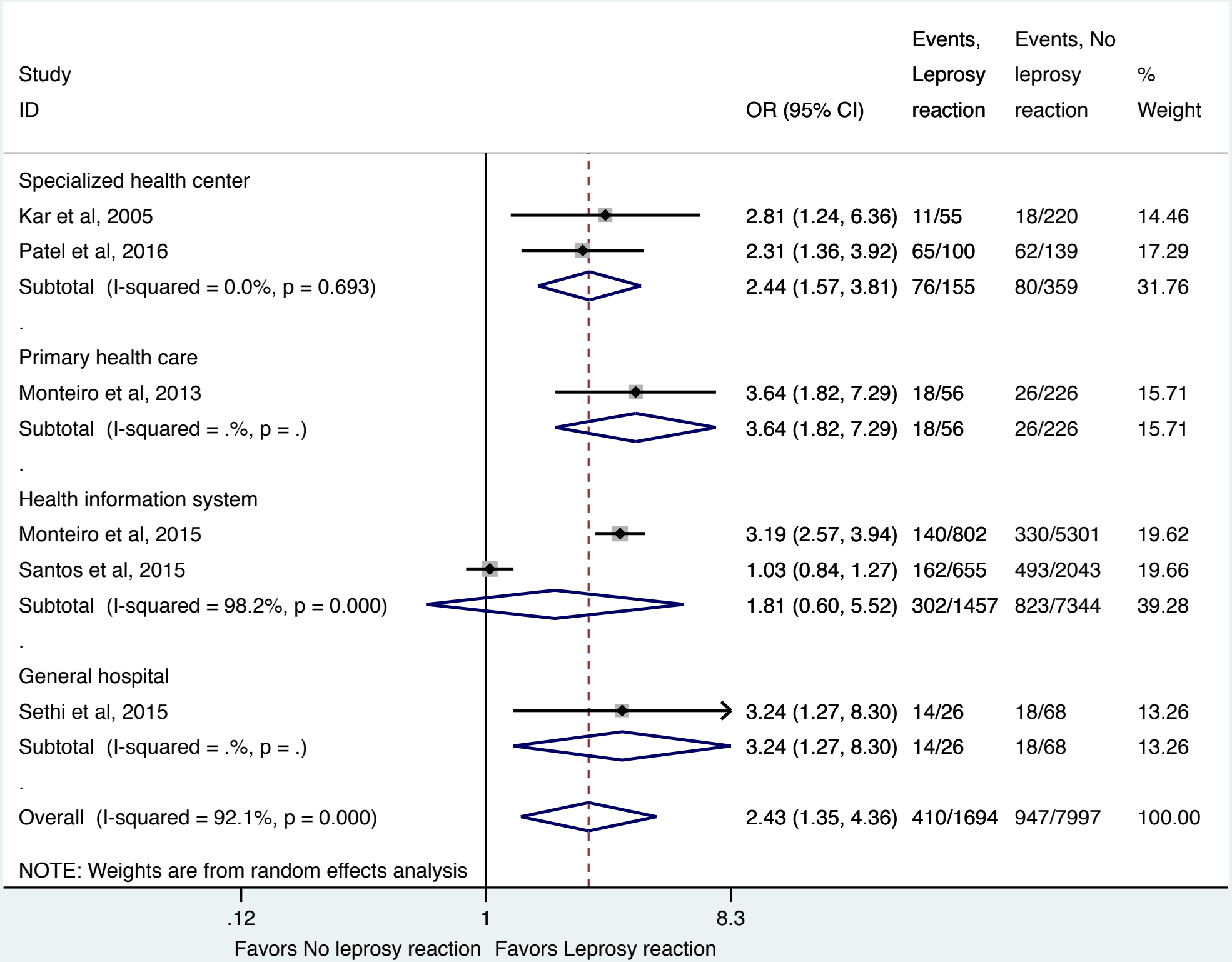
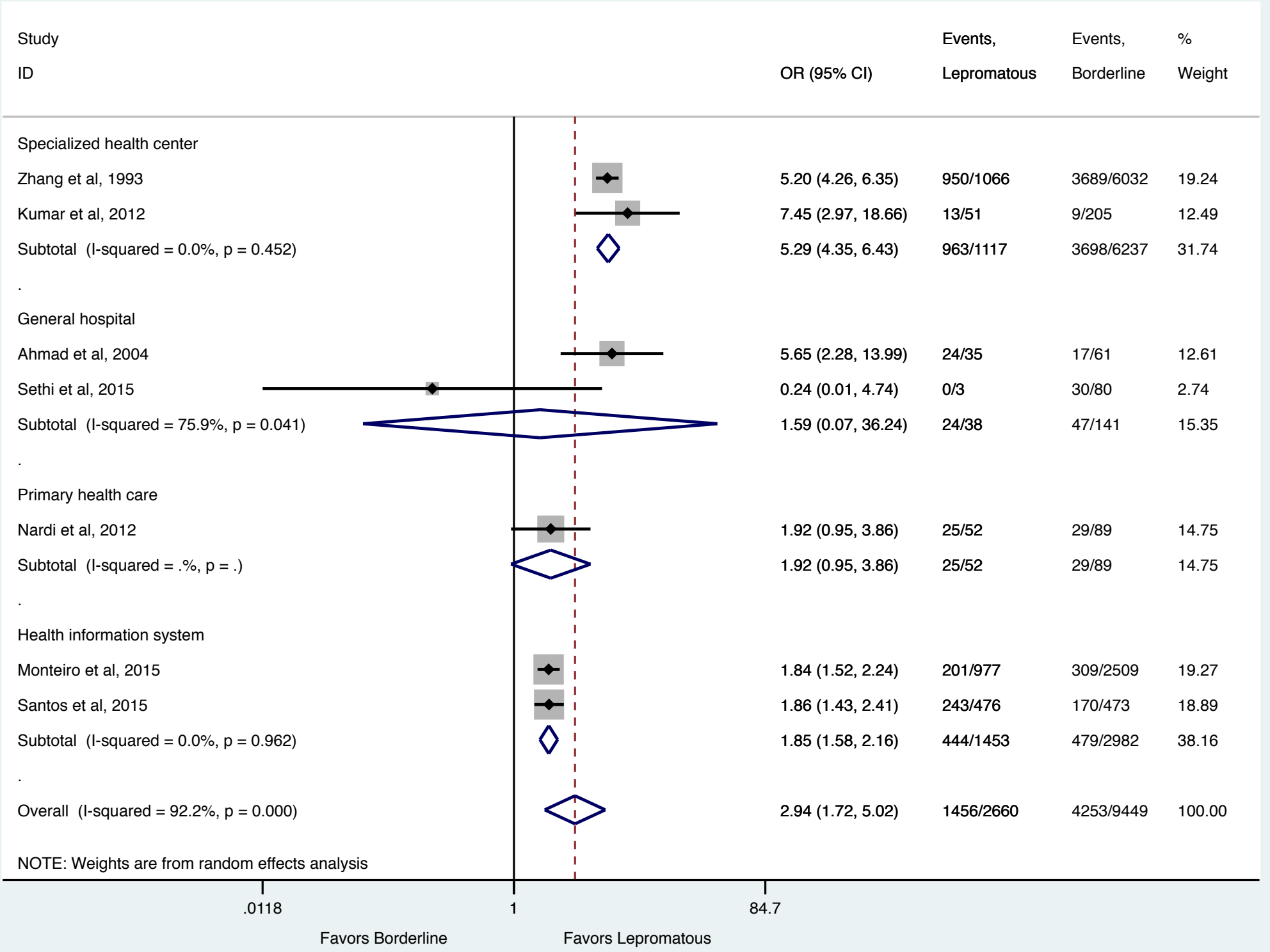
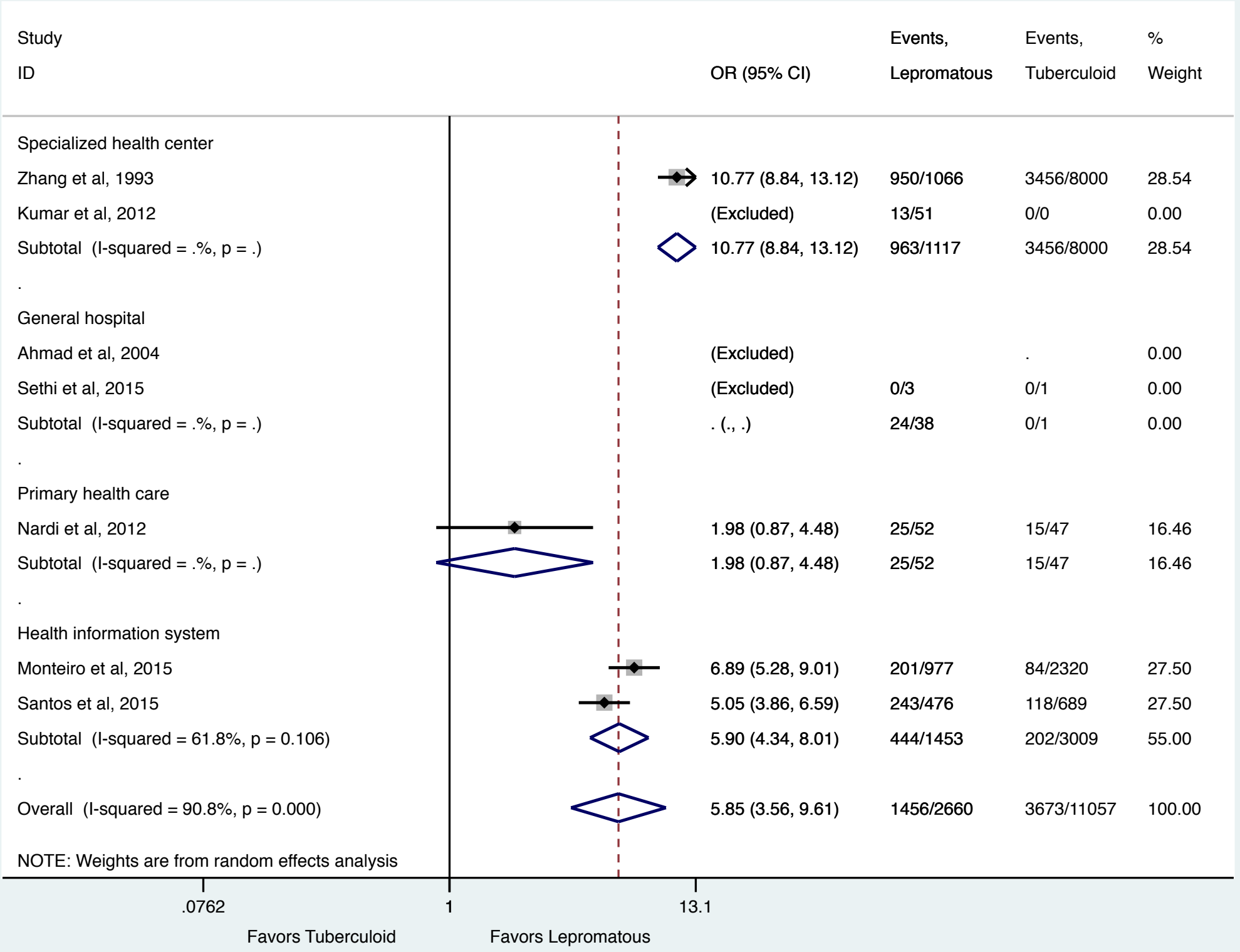
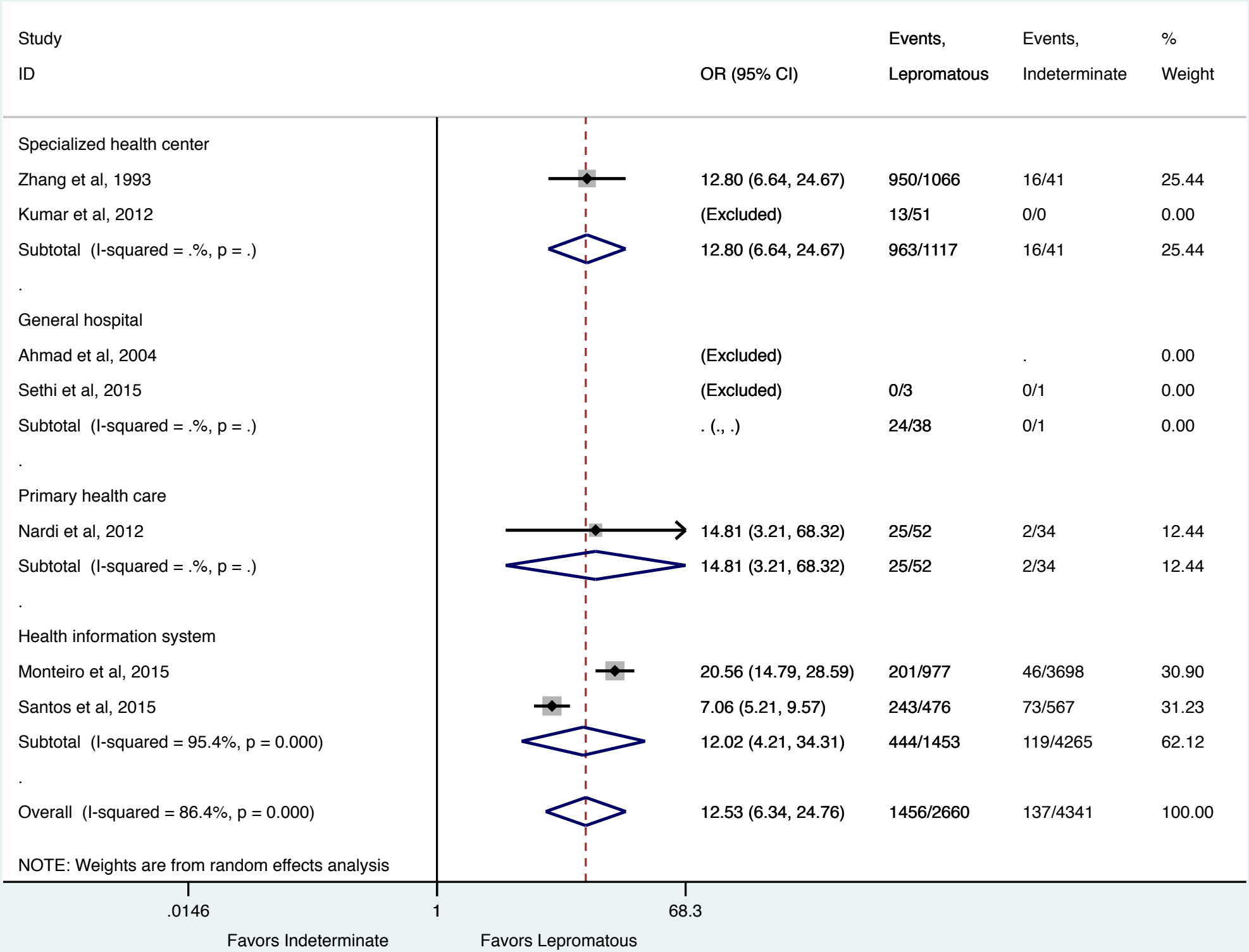
192
Favors PB leprosy
Favors MB Leprosy


Study ID
OR (95% CI)
Events, Leprosy reaction
Events, No leprosy reaction
% Weight
Specialized health center
Kar et al, 2005 2.81 (1.24, 6.36) 11/55 18/220 14.46
Patel et al, 2016 2.31 (1.36, 3.92) 65/100 62/139 17.29
Subtotal (I-squared = 0.0%, p = 0.693) 2.44 (1.57, 3.81) 76/155 80/359 31.76
Primary health care
Monteiro et al, 2013 3.64 (1.82, 7.29) 18/56 26/226 15.71
Subtotal (I-squared = .%, p = .) 3.64 (1.82, 7.29) 18/56 26/226 15.71
Health information system
Monteiro et al, 2015 3.19 (2.57, 3.94) 140/802 330/5301 19.62
Santos et al, 2015 1.03 (0.84, 1.27) 162/655 493/2043 19.66
Subtotal (I-squared = 98.2%, p = 0.000) 1.81 (0.60, 5.52) 302/1457 823/7344 39.28
General hospital
Sethi et al, 2015 3.24 (1.27, 8.30) 14/26 18/68 13.26
Subtotal (I-squared = .%, p = .) 3.24 (1.27, 8.30) 14/26 18/68 13.26
Overall (I-squared = 92.1%, p = 0.000) 2.43 (1.35, 4.36) 410/1694 947/7997 100.00
NOTE: Weights are from random effects analysis
.12
1
8.3
Favors No leprosy reaction
Favors Leprosy reaction


Study ID
OR (95% CI)
Events, Lepromatous
Events, Borderline
% Weight
Specialized health center
Zhang et al, 1993
5.20 (4.26, 6.35)
950/1066
3689/6032
19.24
Kumar et al, 2012
7.45 (2.97, 18.66)
13/51
9/205
12.49
Subtotal (I-squared = 0.0%, p = 0.452)
5.29 (4.35, 6.43)
963/1117
3698/6237
31.74
.
General hospital
Ahmad et al, 2004
5.65 (2.28, 13.99)
24/35
17/61
12.61
Sethi et al, 2015
0.24 (0.01, 4.74)
0/3
30/80
2.74
Subtotal (I-squared = 75.9%, p = 0.041)
1.59 (0.07, 36.24)
24/38
47/141
15.35
.
Primary health care
Nardi et al, 2012
1.92 (0.95, 3.86)
25/52
29/89
14.75
Subtotal (I-squared = .%, p = .)
1.92 (0.95, 3.86)
25/52
29/89
14.75
.
Health information system
Monteiro et al, 2015
1.84 (1.52, 2.24)
201/977
309/2509
19.27
Santos et al, 2015
1.86 (1.43, 2.41)
243/476
170/473
18.89
Subtotal (I-squared = 0.0%, p = 0.962)
1.85 (1.58, 2.16)
444/1453
479/2982
38.16
.
Overall (I-squared = 92.2%, p = 0.000)
2.94 (1.72, 5.02)
1456/2660
4253/9449
100.00
NOTE: Weights are from random effects analysis
.0118
1
84.7
Favors Borderline
Favors Lepromatous


Study
ID
OR (95% CI)
Events, Lepromatous
Events, Tuberculoid
% Weight
Specialized health center
Zhang et al, 1993
10.77 (8.84, 13.12)
950/1066
3456/8000
28.54
Kumar et al, 2012
(Excluded)
13/51
0/0
0.00
Subtotal (I-squared = .%, p = .)
10.77 (8.84, 13.12)
963/1117
3456/8000
28.54
.
General hospital
Ahmad et al, 2004
(Excluded)
.
0.00
Sethi et al, 2015
(Excluded)
0/3
0/1
0.00
Subtotal (I-squared = .%, p = .)
. (., .)
24/38
0/1
0.00
.
Primary health care
Nardi et al, 2012
1.98 (0.87, 4.48)
25/52
15/47
16.46
Subtotal (I-squared = .%, p = .)
1.98 (0.87, 4.48)
25/52
15/47
16.46
.
Health information system
Monteiro et al, 2015
6.89 (5.28, 9.01)
201/977
84/2320
27.50
Santos et al, 2015
5.05 (3.86, 6.59)
243/476
118/689
27.50
Subtotal (I-squared = 61.8%, p = 0.106)
5.90 (4.34, 8.01)
444/1453
202/3009
55.00
.
Overall (I-squared = 90.8%, p = 0.000)
5.85 (3.56, 9.61)
1456/2660
3673/11057
100.00
NOTE: Weights are from random effects analysis
.0762
1
13.1
Favors Tuberculoid
Favors Lepromatous


Study ID
OR (95% CI)
Events, Lepromatous
Events, Indeterminate
% Weight
Specialized health center
Zhang et al, 1993 12.80 (6.64, 24.67) 950/1066 16/41 25.44
Kumar et al, 2012 (Excluded) 13/51 0/0 0.00
Subtotal (I-squared = .%, p = .) 12.80 (6.64, 24.67) 963/1117 16/41 25.44
.
General hospital
Ahmad et al, 2004 (Excluded) . 0.00
Sethi et al, 2015 (Excluded) 0/3 0/1 0.00
Subtotal (I-squared = .%, p = .) . (., .) 24/38 0/1 0.00
.
Primary health care
Nardi et al, 2012 14.81 (3.21, 68.32) 25/52 2/34 12.44
Subtotal (I-squared = .%, p = .) 14.81 (3.21, 68.32) 25/52 2/34 12.44
.
Health information system
Monteiro et al, 2015 20.56 (14.79, 28.59) 201/977 46/3698 30.90
Santos et al, 2015 7.06 (5.21, 9.57) 243/476 73/567 31.23
Subtotal (I-squared = 95.4%, p = 0.000) 12.02 (4.21, 34.31) 444/1453 119/4265 62.12
.
Overall (I-squared = 86.4%, p = 0.000) 12.53 (6.34, 24.76) 1456/2660 137/4341 100.00
NOTE: Weights are from random effects analysis
.0146
1
68.3
Favors Indeterminate
Favors Lepromatous